

## REMARKS

Claims 11-16 and 19-30 are pending in the application. Claims 20, 23-25, and 28 are withdrawn as being directed to nonelected species. In the Office Action mailed January 27, 2009, claims 11-16, 19, 21, 22, 26, 27, 29, and 30 are rejected under 35 U.S.C. 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

### **I. Rejections under 35 U.S.C. 112, second paragraph**

Claims 11-16, 19, 21, 22, 26, 27, 29, and 30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite. The Applicants respectfully traverse the rejections. As a preliminary matter, although not stated in the Action, the Applicants have presumed in this response that claims 14-16, 19, 22, 27, and 30 are rejected solely for being dependent upon a rejected base claim.

In particular, independent claim 11 is rejected as being indefinite because “[s]ince step b) does not indicate which way can be used to decrease the relative amount of any nucleic acid molecules that contain errors, it is unclear why error-free nucleic acid molecules from said plurality or pool can be selectively amplified thereby decreasing the relative amount of any nucleic acid molecules that contain errors”. Independent claim 11 has herein been amended in order to recite a step of distinguishing between error-free and error-containing nucleic acid molecules within said plurality or pool and to clarify that the step of selectively amplifying amplifies only the error-free nucleic acid molecules from said plurality or pool, thereby decreasing the percentage of error-containing nucleic acid molecules within said plurality or pool. Dependent claim 14 has been amended to specify the particular step of underlying base claim 11 that is modified by the limitation of claim 14. Support for these amendments is found particularly in paragraph [0150] and in Figs. 6A-C and 17, with further support found at least at paragraphs [0032], [0033], [0107]-[0110], [0113], and [0145] -[0149]. No new matter is added by these amendments, entry of which is therefore respectfully requested. The Applicants particularly note that methods of distinguishing between error-free and error-containing nucleic acid molecules are well-known in the art, as are methods of selectively amplifying particular subsets of nucleic acid molecules within a pool, and that many such methods are both discussed and incorporated by reference into the Applicants’ Specification [see, for example, paragraph [0032]]. The Applicants therefore believe that the amendment made herein to claim 11 has

resolved the indefiniteness issue raised by the rejection, and that claim 11, as amended herein, meets the requirements of 35 U.S.C. 112, second paragraph. Reconsideration and withdrawal of the rejection of claim 11 is therefore respectfully requested. Furthermore, because claims 14-16 and 19 depend from currently amended independent claim 11, which is now in condition for allowance, claims 14-16 and 19 are also in condition for allowance. Reconsideration and withdrawal of the rejection of claims 14-16 and 19 is therefore respectfully requested.

Independent claim 12 is rejected as being indefinite because “it is unclear why error in said plurality or pool can be corrected using nucleic acid molecules in said plurality or pool as a template”. Independent claim 12 has herein been amended in order to recite a step of distinguishing between error-free and error-containing nucleic acid molecules within said plurality or pool and to clarify that the step of correcting errors uses error-free nucleic acid molecules in said plurality or pool as a template for repair of said error-containing nucleic acid molecules. Support for these amendments is found in particular at paragraphs [0107]-[0110], [0152], and [0155]-[0160] and in Figs. 19 and 20A-B, with further support found at least at paragraphs [0032]-[0034], [0113], and [0145] -[0151]. No new matter is added by these amendments, entry of which is therefore respectfully requested. The Applicants note that methods of distinguishing between error-free and error-containing nucleic acid molecules are well-known in the art, as are methods of nucleic acid repair and/or construction using a template, and that such methods are both discussed and incorporated by reference into the Applicants’ Specification [see, for example, paragraphs [0032], [0107], and [0145]]. The Applicants therefore believe that the amendment made herein to claim 12 has resolved the indefiniteness issues raised by the rejections, and that claim 12, as amended herein, meets the requirements of 35 U.S.C. 112, second paragraph. Reconsideration and withdrawal of the rejection of claim 12 is therefore respectfully requested.

Independent claim 13 is rejected as being indefinite because “it is unclear which way can be used to remove errors from portions of said nucleic acid molecules and yield nucleic acid molecules having an error-free sequence”. Independent claim 13 has herein been amended in order to recite a step of identifying error-containing ones of said nucleic acid molecules and to clarify that, in the step of removing, the error-containing portions of the error-containing nucleic acid molecules are removed to produce error-free nucleic acid sequences and that, in the step of recombining, error-free nucleic acid sequences are combined to yield error-free nucleic acid molecules. Support for this amendment is found in particular at least at paragraphs [0151],

[0153]-[0160], and [0166]-[0171] and in Figs. 19, 20A-B, 22, and 23A-B, and that further support is found at least in paragraphs [0032]-[0034], [0113], [0145] -[0150], and [0152]. No new matter is added by this amendment, entry of which is therefore respectfully requested. The Applicants note that methods of identifying error-containing nucleic acid molecules are well-known in the art, as are methods of removing specific portions of nucleic acid molecules and of combining nucleic acid sequences to form nucleic acid molecules, and that many such methods are both discussed and incorporated by reference into the Applicants' Specification [see, for example, paragraphs [0032], [0107], and [0145]]. The Applicants therefore believe that the amendment made herein to claim 13 has resolved the indefiniteness issues raised by the rejections, and that claim 13, as amended herein, meets the requirements of 35 U.S.C. 112, second paragraph. Reconsideration and withdrawal of the rejection of claim 13 is therefore respectfully requested. Furthermore, claim 30 depends from currently amended independent claim 13, which is in condition for allowance, claim 30 is also in condition for allowance. Reconsideration and withdrawal of the rejection of claim 30 is therefore also respectfully requested.

Dependent claims 21 and 26 are rejected as being indefinite because "it is unclear that the step of correcting errors [removing errors] comprises the step of mismatch cleavage and recognition of what". Dependent claim 21 has herein been amended in order to recite that the step of correcting errors comprises the steps of mismatch recognition on the error-containing nucleic acid molecules to identify specific base errors in the molecules, cleavage of the base errors, and replacement of the base errors with the correct bases according to the template. Dependent claim 26 has herein been amended in order to recite that the step of removing errors comprises the steps of mismatch recognition on the error-containing nucleic acid molecules to identify specific base sequence errors in the error-containing nucleic acid molecules and cleavage of said specific base sequence errors. Dependent claims 22 and 27 have been amended to reflect the changes to their underlying base claims. Support for these amendments is found at least at paragraphs [0032]-[0034], [0107]-[0109], [0145] -[0150], [0152], [0153], [0155]-[0160], and [0169]-[0171] and in Figs. 16A-B, 17, 19, 20A-B, 22, and 23A-B. No new matter is added by these amendments, entry of which is therefore respectfully requested. The Applicants note that methods of mismatch cleavage and recognition are well-known in the art and that such methods are both discussed and incorporated by reference into the Applicants' Specification [see, e.g., paragraphs [0034], [0107], and [0145]]. The Applicants therefore believe that the

amendments made herein to claims 21 and 26 have resolved the indefiniteness issues raised by the rejections, and that claims 21 and 26, as amended herein, meet the requirements of 35 U.S.C. 112, second paragraph. Reconsideration and withdrawal of the rejection of claims 21 and 26 is therefore respectfully requested. Furthermore, because claim 21 depends from currently amended independent claim 12, which is now in condition for allowance, claim 21 is also in condition for allowance. Because claim 26 depends from currently amended independent claim 13, which is now in condition for allowance, claim 22 is also in condition for allowance. Reconsideration and withdrawal of the rejections of claims 21 and 26 is therefore also respectfully requested. In addition, because claim 22 depends from currently amended claim 21, which is now in condition for allowance, claim 22 is also in condition for allowance. Reconsideration and withdrawal of the rejection of claim 22 is therefore respectfully requested. Because claim 27 depends from currently amended claim 26, which is now in condition for allowance, claim 27 is also in condition for allowance. Reconsideration and withdrawal of the rejection of claim 27 is therefore respectfully requested.

Dependent claim 29 is rejected because there is insufficient antecedent basis for the limitation “the separated action” because there is no phrase “separated action” in the base claim (claim 13) and as being vague and indefinite because “it is unclear why the separate action of a mismatch binding protein and a nuclease (i.e. by interacting with what) can be used to remove errors”. Dependent claim 29 has herein been amended in order to remove the phrase “the separate action of” and to recite that the step of removing errors is performed by a mismatch binding protein to identify specific base sequence errors in the error-containing nucleic acid molecules and a nuclease to cleave the specific base sequence errors. Support for this amendment is found at least at paragraphs [0032], [0034], [0107], [0145] -[0148], [0155]-[0160], and [0169]-[0171] and in Figs. 16A-B, 19, 20A-B, 22, and 23A-B . No new matter is added by this amendment, entry of which is therefore respectfully requested. The Applicants note that the uses of mismatch binding proteins and nucleases are well-known in the art and that such uses are both discussed and incorporated by reference into the Applicants’ Specification [see, for example, paragraphs [0032], [0034], and [0107]]. The Applicants therefore believe that the amendment made herein to claim 29 has resolved the indefiniteness issues raised by the rejections, and that claim 29, as amended herein, meets the requirements of 35 U.S.C. 112, second paragraph. Reconsideration and withdrawal of the rejection of claim 29 is therefore respectfully requested. Furthermore, because claim 29 depends from currently amended

independent claim 13, which is in condition for allowance, claim 29 is also in condition for allowance. Reconsideration and withdrawal of the rejection of claim 29 is therefore also respectfully requested.

The indefiniteness issues being resolved, the Applicants respectfully submit that claims 11-16, 19, 21, 22, 26, 27, 29, and 30 are neither anticipated nor rendered obvious by any art of record, none of which teaches removal and control of errors in nucleic acid molecules having a user-specified sequence and length and synthesized by the specific process of the Applicants, in combination with the other claimed elements of the Applicants invention, as recited in currently amended independent claims 11-13. Allowance of claims 11-16, 19, 21, 22, 26, 27, 29, and 30 is therefore respectfully requested.

### **II. Conclusion**

Claims 11-14, 21, 22, 26, 27, and 29 have been amended. No new matter is presented by these amendments. The Applicants respectfully submit that claims 11-16, 19, 21, 22, 26, 27, 29, and 30 are now in condition for allowance, which action is now requested. Furthermore, the generic claims being allowable, the Applicants respectfully request rejoinder and allowance of the nonelected species claims.

For this reason, and in view of the foregoing arguments, the Applicants believe that this application is now in condition for allowance, which action is respectfully solicited. Should there remain any unresolved issues, it is requested that the Examiner telephone Norma E. Henderson, Applicants' Attorney, at 603-437-4400, so that such issues may be resolved as expeditiously as possible.

Respectfully Submitted,



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Norma E. Henderson

Date

Attorney/Agent for Applicants

Reg. No. 39,219

Henderson Patent Law

13 Jefferson Drive

Tel/Fax: 603-437-4400

Londonderry, NH 03053-3647

[normahenderson@comcast.net](mailto:normahenderson@comcast.net)